REMARKS

I. Status of the Claims

Claims 69-92 and 94-96 have been withdrawn from consideration as drawn to non-elected species. Claims 55-65 and 67-96 are currently in the case.

II. Objection to the Specification

The Actions objects to the Specification on the ground that essential material is incorporated by reference from pending applications 08/979,456, 08/979,526, and 09/198,998, and that there is an attempt to incorporate this material that is allegedly ineffective.

Applicant assumes the Examiner is referring to the paragraph beginning on page 9, line 8 that continues on page 9, and the paragraph immediately following, which refer to the applications mentioned in the Action. Applicant submits that the disclosures of these three applications are properly incorporated by reference in the originally filed application in the first paragraph, on page 1 of the application. Applicants request, therefore, withdrawal of the objection to the specification., and further note that should the addition to the present application of material from any of these applications be deemed to be necessary, that such addition would not constitute new matter. (MPEP 2163.07(b))

III. Rejections Under 35 USC §112

The Action rejects claims 55-65, 67, 68, and 93 under 35 USC 112, first paragraph for lack of written description for the claims element "about 90% of said water soluble peptides are between about 300 and about 1300 daltons in molecular weight."

Applicant respectfully traverses in that the specification provides more than adequate written description for the claim element. First, as stated in the Action, the claim element is in the originally filed claims, both in the present application and in the parent. It is established

patent law that "original claims constitute their own written description.) *In re Koller*, 613 F2d 819, 204 USPQ 702 (CCPA 1980) (MPEP 2163).

The Specification provides further support at the paragraph at the bottom of page 8 and top of page 9. This paragraph describes the characteristics of the peptides and the analysis of the molecular weight based in part on the data in Figure 1. The claim element is a reasonable assessment of the molecular weight of those peptides based at least in part on the data of Figure 1. As such, one of skill in the art would fully understand that the inventors had possession of the invention of claim 55 at the time of filing of the present application, as well as at the time of filing of the parent. The Specification thus contains more than adequate written description for the claims and Applicant respectfully requests that this rejection be withdrawn.

Claims 55-65, 67 and 68 are also rejected under §112, first paragraph for alleged lack of enablement for any composition other than a topical composition. Applicants respectfully traverse on the ground that the Specification fully enables one of skill in the art to produce the claimed peptides. The claimed peptide compositions, which the Action acknowledges as being novel and as having at least one utility, for use in topical formulations, is fully enabled.

Applicant does not agree with the Action's assessment of the nature of the invention. The invention of claim 55 is the powdered peptide composition. The composition is shown in the application to have useful bioactivity. The Action's interpretation of the invention as limited to a topical composition reads a limitation into the claims that is not there.

The cases cited by the Action are not relevant to the present claims. For example, the Action states that "in cases involving chemicals and chemical compounds that differ radically in their properties... that the chemicals or chemical compositions *included in the claims* are capable of achieving the desired result." (emphasis added) Applicant submits that the present claims are not drawn to chemicals or chemical compounds that differ radically in their properties, but rather

are drawn to a composition of keratin peptides that are shown in the Specification to have bioactivity.

The issue here is not whether the Specification enables all compositions to which the peptide composition can be added, but rather, the enablement of the peptide composition independent of adding it to a particular type of carrier. The Specification contains more than adequate description of how to obtain the peptide composition and also teaches how to use the composition to stimulate growth of useful cell types. Nothing more is required for enablement of the claims. Applicant submits, therefore, that this rejection is improper and requests that the rejection be withdrawn.

II. Claim rejections under 35 U.S.C. §103

Applicant submits that none of the cited references teaches or suggests the claimed inventions. The Action cites several references that refer to keratin and keratin products. None of these references, however, describes the peptide compositions of the present claims. The present application arises from the surprising discovery that after a mild oxidation of hair, a water soluble portion of the oxidized product contains a fraction of peptides that have bioactivity. This fraction was discovered by subjecting a neutralized solution of oxidized keratin protein to alcohol precipitation at a concentration at which low molecular weight peptides precipitate from solution. These peptide compositions were then shown to have the ability to stimulate growth of cells that are involved in wound healing. None of the cited keratin art suggests the presence of these low molecular weight peptides in a keratin preparation, but rather describe larger molecular weight fractions of MW 30,000 and above. In those references in which some wound healing properties are described for keratin compositions, there is no suggestion that the claimed low molecular weight fraction exists, or that such a fraction, if it did exist would exhibit wound healing properties. The only low molecular weight keratin product described is a hydrolysate in

which either harsh reaction conditions or enzymes are used to break the peptide bonds of the protein backbone. In contrast, the conditions under which the claimed peptide compositions are produced are chosen to minimize such hydrolysis.

The Action also cites a reference describing peptides isolated from milk proteins. There is no suggestion and no reason to believe that the milk peptides are in any way related to the keratin peptides of the claims. There is also suggestion in the reference that similar sized peptides from any other source would have a similar activity to those isolated from milk proteins. There is no motivation to combine this reference with the description of peptide compositions from any other source. The Examiner has thus failed to make a *prima facie* case of obviousness and the rejections under §103 should be withdrawn.

The claimed compositions are neither taught nor suggested by the '173 patent.

The Action rejects claims 55-65, 67, 68, and 93 as obvious over US 4,495,173, taking the position that the product produced by the method described in the '173 patent could have a molecular weight of 200-5000. Applicant does not agree that the oxidized composition described in the '173 patent could have a molecular weight of 200-5000, as the '173 patent states that is has a molecular weight of 30,000-100,000 (col. 5, line 47).

The Action states that the '173 patent describes oxidizing human hair, feathers etc with peroxide or peracetic acid followed by neutralization and gel filtration. Applicant assumes the Action is referring to the method described as method (1) Oxidation and Decomposition Reaction in column 2, beginning on line 31. The reaction described is carried out in an excess of oxidizing agent such that all the disulfides are oxidized to sulfonic acids. The '173 patent also states at column 5, line 45

The decomposition products obtained by the method (1) or (2) should preferably have an average molecular weight of 30,000-100,000 and those obtained by the method (3) should

preferably have an average molecular weight of 200-5,000. The '173 patent thus teaches away from the claimed invention, teaching that the oxidation method produces a product of 30,000-100,000 molecular weight. Nowhere does the '173 patent suggest that a low molecular weight fraction is produced by this method, nowhere does the '173 patent teach of suggest a peptide fraction of from 300-1300 daltons, and nowhere does the '173 patent suggest that such a fraction, if it did exist, would have bioactivity. The Examiner has thus failed to make a prima facie case of obviousness and this rejection should be withdrawn.

This oxidative method is again discussed in the '173 patent in Synthetic Example 1 column 9, line 10. In the example, the wool is oxidized, filtered and then dissolved in ammonia solution. The product is then taken to pH 4 "**whereupon α-keratose was settled as a precipitate.**" (emphasis added) As discussed in the response to the previous Office Action, α-keratose is a known fraction of molecular weight 30,000-60,000 that is insoluble at low pH. This fraction is thus precipitated by bringing the solution to pH below 4. This is a different fraction than the low molecular weight peptides that are precipitated by alcohol as described in the present application and claims. The Examiner has ignored the acid precipitation step and instead has chosen certain steps from the oxidation method (method (1) of the '173 patent) and combined them with results from the enzymatic degradation method (method (3) of the '173 patent) in an attempt to reconstruct Applicant's invention in hindsight.

Turning to the enzymatic process, (process (3)) the '173 patent teaches that hydrolysis with an enzyme, with strong acid, and in strong base, all resulted in peptide fractions in which the disulfide bonds were intact, in contrast to the oxidation method (1) in which all the cystines were converted to sulfonic acid. That alone is a chemical characteristic that distinguishes the claimed compositions from the hydrolysates of the '173 patent. Furthermore, a peptide composition with an average molecular weight of from 200-5,000 does not suggest the

composition of the present claims, in which at least 90% of the peptides have a molecular weight of from 300-1300, with an average of about 850 daltons. And again, there is no suggestion in the '173 patent that the hydrolysates have any bioactivity. The Action states that the process of production does not impart patentability, but that is a moot point since the peptide compositions of the present claims are not anticipated by the cited art.

Applicants submit therefore, that the '173 patent can in no way be said to teach or suggest the claimed inventions, that the '173 patent teaches away from the claimed invention, and that all rejections over the '173 should be withdrawn.

The claimed compositions are neither taught nor suggested by the '138 patent.

The Action also rejects claims 55-65, 67, 68, and 93 as obvious over 5,276,138 ('138) in view of 6,506,732 ('732). Applicant traverses and finds no description or suggestion of the present invention in the cited references.

The '138 patent has been addressed in the response to the previous Office Action. The patent describes a composition containing α-keratose. α-keratose is an acidic portion of the oxidized hair that is insoluble at low pH, and thus precipitates in acid. This fraction has a much higher molecular weight than the peptides precipitated by ethanol at neutral pH as described in the present specification and claims. Figure 1 of the '138 shows the molecular weight, which has a peak around 30-40,000. Even if the peptides of the present claims were contained within the composition with the larger peptides of the '138 preparation, there is no way to know that from reading the patent. There is also no suggestion in the patent that there is a low molecular weight fraction that could be isolated, or that any fraction of this preparation would have the cell growth activity of the claimed compositions.

The '138 reference does not suggest that any useful fraction of peptides can be precipitated from a soluble preparation of oxidized hair. The '138 does teach that a fraction can be precipitated by lowering the pH of the solution to below 4. For example,

> As previously stated, the present invention relates also to the process for recovering the solubilized product of the animal hairs which comprises admixing the solution of said product with an organic acid or an aqueous solution thereof to precipitate said product. ('138) column 4, lines 29-33
>
> Under normal conditions, the pH of the mixed system of the solution of the solubilized product of the animal hairs and the organic acid may be adjusted less than about 4.5, preferably 1-4. If the pH of the mixed system if more than 4.5, the solubilized product of the animal hairs becomes hard to precipitate. (col. 4, lines 58-63)

Thus the '138 reference also teaches away from the present claims, by teaching that the composition cannot be precipitated at pH above 4.5, and yet the claimed peptides are precipitated at neutral pH. Thus the claims are clearly distinguished from the disclosure of '138, both in the process of obtaining them and in their molecular weight, not just because of the process step alone, but because the different chemical characteristics of the two peptide compositions cause them to precipitate under different conditions.

Although the '138 patent discusses the use of a polar solvent such as alcohols, acetone and the like, this step is used to further purify the α-keratose that was the result of a previous acid precipitation and to "remove trace amounts of stinking components of low molecular weight, colored substances and the like contained in the solubilized product solution of the animal hairs," (col 5, line 24)and not to isolate a bioactive subfraction of peptides. The '138 can thus in no way be said to teach or suggest the present claims, and teaches away from the present claims by teaching precipitation from aqueous solution at low pH, and by teaching that only trace amounts of useless contaminants can be removed from the α-keratose preparation by washing

with aqueous solution of organic acids and/or volatile organic solvents. Therefore, the low molecular weight peptides would not meet the objects of the '138 disclosure. According to M.P.E.P. 2143.01, if, as in the present case, a modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).Applicant requests therefore, that all rejections over '138 be withdrawn.

All rejections over '138 in view of '732 should be withdrawn as the references are not combinable and would not reach the claimed inventions even if combined.

The disclosure of the '732 patent in no way overcomes the deficiencies of the '138 reference as applied to the claimed inventions. The Examiner has completely failed to make a *prima facie* case of obviousness for the combination of references. The '732 reference describes compositions including peptides derived from milk proteins that are totally unrelated to the α-keratose described in '138. The Examiner has pointed to nothing in the references that would suggest any combination or any reason to modify the disclosures of either reference for such a combination.

Establishing *prima facie* obviousness requires a showing that each claim element is taught or suggested by the prior art. *See* In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Specifically, establishing *prima facie* obviousness requires a showing that some combination of objective teachings in the art and/or knowledge available to one of skill in the art would have lead that individual to arrive at the claimed invention. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). Moreover, establishing *prima facie* obviousness requires not only a showing that such a combination of prior art teachings is possible, but also that the teachings would have 1) motivated the skilled artisan to make the combination to arrive at the claimed invention, and 2) suggested to the skilled artisan a reasonable likelihood of success in making

and using the claimed invention. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). Absent a showing of such motivation and suggestion, *prima facie* obviousness is not established. *See Fine*, 5 USPQ2d at1598. Additionally, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20USPQ2d 1438 (Fed. Cir. 1991)

Therefore, even if the references were to teach every element of the claimed invention, which they do not, without a motivation to combine the references, there is no *prima facie* case and no burden on Applicant to present evidence of non-obviousness. The Action appears to take the position that any peptide is equivalent to any other peptide of the same or similar molecular weight regardless of the source or the amino acid sequences. Otherwise there would be no connection between the '732 disclosure and the present claims, and even given that erroneous idea, there is no connection between the '138 and '732 references except they both describe peptide compositions.

Turning to the '732 patent, Applicant finds no suggestion in the reference that one should modify the processes to oxidize disulfide bonds as in the '138 patent. Applicant finds no mention of disulfide bonds at all in the '732, or any other reason to oxidize the proteins in order to isolate the described peptides. The '732 rather describes enzymatic hydrolysis with pepsin and chymotrypsin in order to obtain peptides with specific characteristics. There is no suggestion in the '732 that the same or similar peptides could be obtained from hair, from an isolated α-keratin fraction as described in '138, or any other keratin source. Applicant finds, therefore, no motivation to combine the references, and no understanding of how such a combination would arrive at the claimed invention.

Because the '138 and '732 references do not teach every element of the claims, contain no motivation within their respective disclosures to combine the teachings of the references in any

way, and further because one of skill in the art would have no expectation of succeeding in arriving at the claimed inventions in making such a combination, the current rejection is improper. Applicant respectfully requests that all rejections over '138 and '732 either separately or in combination be withdrawn.

The '583 patent does not describe or suggest any of the process steps in the claims nor any peptide product of the claims and can in no way be said to teach or suggest the claimed inventions.

The Action rejects claims 55-65, 67, 68, and 93 as obvious over US Patent No. 5,763,583 ('583) in view of '732. The Action states that '583 teaches a water soluble protein ... produced by oxidation, neutralization of the produced aqueous solution, followed by filtration, and the use of organic solvents. Applicant traverses and submits that this is nothing more picking out process steps in an attempt to reconstruct Applicant's claims with no regard for how or when those steps are used and for what purpose in the production of the products of the '583 reference. For example, the only use of organic solvents is for solutions of plasticizers for making films as described in col 5 and in Example 4 for the same purpose. There is no way that the use of an organic solvent as described in '583 is equivalent to, or in any way suggests the precipitation of low molecular weight peptides from aqueous solution in alcohol as in the present claims.

Furthermore, the '583 does not describe "oxidizing human or animal hair, human or animal nails, fur, hooves, or feathers, in an aqueous oxidizing solution" as in claim 55, but rather instead describes oxidation of the thioglycolate groups bound to the protein by the previous reduction of the cystine disulfide bonds.

> In accordance with the present invention, disulfide bonds (-SS-) in the disulfide bond-containing water-insoluble protein are reduced into mercapto groups (-SH) and a part or entire portion of the mercapto groups is subsequently converted into carboxymethyldisulfide groups (-SSCH2COOH), whereby the solubilized protein is obtained. (col 2, line 49)

The product of the reduction and oxidation reactions in '583 may be filtered to remove insoluble materials, but the patent also teaches that the product is dialysed to remove any molecules with a molecular weight under 10,000. (col. 4, line 16-20, col. 6, lines 47-49, col. 7, lines 14-17, col. 8, lines 25-28) This results in protein products having molecular weights of 40,000-60,000. (col 4, line 30) 40,000-80,000 (Examples 1 and 2) The dialysis step thus removes and discards any peptides that would fall within the claimed compositions in the present application. This is a desired object of the '583 disclosure to remove low molecular weight products. As stated in col. 4, lines 30-33, no lower molecular weight products were detected in the SDS gels. Additionally, the first paragraph in Column 2 states that it is an objective of the invention to "maintain the molecular weight and the α-helix structure of the keratin protein." The '583 thus also teaches away from the claimed invention by teaching the benefit of products that exclude the peptide products of the instant claims.

Any attempt to combine the '583 with the '732 disclosure suffers the same deficiencies as discussed above for the combination with '138. The references are unrelated and contain no direction of motivation for any combining of the teachings. The Examiner has simply failed to make any kind of credible case for obviousness. Applicant respectfully requests that all rejections over the '583 alone or in combination with other references be withdrawn.

The '552 patent does not teach or suggest the elements of the present claims and teaches away from any composition of low molecular weight peptides.

The Action rejects claims 55-56, 67, 68, and 93over US 5,932,552 in view of '732, taking that position that the description of certain process steps that appear in the claims renders those claims obvious. Applicant respectfully traverses on the ground that following the processes

described in the '552 patent result in a very different product that in no way suggests, but rather teaches away from the present claims.

The '552 reference again describes protein fractions from keratin containing materials that are of much higher molecular weight than those of the present claims. The peptides of the present claims would, in fact, be inoperable in the practice of the '552 patent, as no hydrogel can be formed from the low molecular weight peptides of the present claims. The Examiner's attention is drawn to the description in columns 3 and 4. The hair is oxidized and filtered to remove the insoluble materials and dried (col 3, lines 47-65). The soluble material is then reduced with ammonium thioglycolate at high pH (3N ammonium hydroxide). This step is totally ignored by the present Action. After this step the solution is again filtered to remove the β fraction (col. 4, line23). The next step is also ignored by the present Action.

> The supernatant is purified, using a method such as dialysis. A preferred method uses dialysis against running water using a dialysis membrane (Spectra/Por TM) having a cutoff of about 8000 MW. (col. 32-35)

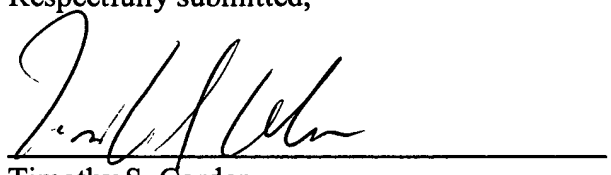
The '552 thus teaches that anything below 8000 molecular weight is discarded, sent down the drain with the running water from the dialysis. The reference thus clearly teaches away from the present claims and is not combinable with any of the other cited references to make a case for obviousness against the present claims. Applicant respectfully requests that all rejections over '552 be withdrawn.

In light of the preceding discussion, the Examiner has completely failed to make a prima facie case of obviousness and Applicant respectfully requests that all rejections under §103 be withdrawn.

Conclusion

In light of the preceding discussion, all pending claims are in condition for allowance and an early indication of such is respectfully requested. Applicant further requests that the withdrawn claims be rejoined to the Application in the allowance. If the Examiner has any questions or suggestions, she is invited to call to the undersigned representative at 512.542.8446.

Respectfully submitted,



Timothy S. Corder
Reg. No. 38,414
Agent for Applicants

Vinson & Elkins L.L.P.
First City Tower
1001 Fannin, Suite 2300
Houston, Texas 77002-6760
512.542.8446

Date: September 7, 2005